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Original Research Article

A Comparative Study Between Intrathecal Nalbuphine Vs Intrathecal Buprenorphine As An Adjuvant To Intrathecal Bupivacaine for Post Operative Analgesia in Patients Undergoing Lower Abdominal and Lower Limb Surgeries Under Spinal Anaesthesia

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Abstract:

Background: Intrathecal opioids are commonly used as adjuvants to local anaesthetics during spinal anaesthesia to prolong postoperative analgesia and improve block quality. Nalbuphine and buprenorphine have different receptor profiles and may produce different analgesic effects.

Aim: To compare intrathecal nalbuphine and intrathecal buprenorphine as adjuvants to hyperbaric bupivacaine for postoperative analgesia in patients undergoing lower limb surgeries under spinal anaesthesia.

Methods: This comparative study included patients undergoing lower limb surgeries under spinal anaesthesia. Patients were divided into two groups: group BN received intrathecal bupivacaine with nalbuphine, while group BB received intrathecal bupivacaine with buprenorphine. Onset and duration of sensory and motor block, duration of analgesia, time to rescue analgesia, haemodynamic parameters, sedation score, and adverse effects were compared.

Results: Nalbuphine produced significantly earlier onset of sensory and motor blockade. Buprenorphine produced significantly prolonged sensory and motor block, longer duration of analgesia, and delayed rescue analgesic requirement. Haemodynamic parameters remained stable in both groups, and adverse effects were minimal.

Conclusion: Intrathecal buprenorphine was superior for prolonged postoperative analgesia, while nalbuphine provided faster onset of blockade with good safety.

Keywords: Nalbuphine; Buprenorphine; Bupivacaine; Spinal anaesthesia; Postoperative analgesia.

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Introduction

Spinal anaesthesia (SA) is a preferred regional anaesthetic technique for lower limb surgeries because it provides rapid onset, dense sensory and motor blockade, good surgical relaxation, and avoids many disadvantages of general anaesthesia [1]. However, the duration of postoperative analgesia (POA) after intrathecal bupivacaine alone is limited; therefore, adjuvants are commonly added to improve block quality, prolong analgesia, reduce rescue analgesic requirement, and maintain haemodynamic stability [2]. Intrathecal opioids are widely used for this purpose because they act on spinal opioid receptors and produce synergistic analgesia with local anaesthetics [3]. Buprenorphine, a partial μ-opioid receptor agonist with prolonged receptor binding, has been shown to extend POA when combined with hyperbaric bupivacaine [4]. Nalbuphine, a κ-receptor agonist and μ-receptor antagonist, provides effective spinal analgesia with relatively lower risk of μ-mediated adverse effects such as pruritus and respiratory depression [5]. Recent comparative evidence suggests that both nalbuphine and buprenorphine improve POA when used as intrathecal adjuvants, but the better adjuvant for lower limb surgeries remains clinically relevant [1, 4, 5]. The aim of the present study was to compare intrathecal nalbuphine and intrathecal buprenorphine as adjuvants to intrathecal hyperbaric bupivacaine for POA in patients undergoing lower limb surgeries under SA.

Methods

It was a single center prospective, randomized, double blinded, comparative study was conducted in the department of Anesthesiology, NRI Institute of Medical sciences, Sangivalasa, Vishakhapatnam.

Study protocol was approved by institutional ethical committee (Reg. No: M1980103181). Based on Manjula R et al. [6], the calculated minimum sample size was 25 patients per group, using sensory block onset values. Patients aged 18-60 years, either gender with ASA physical status I or II, undergoing lower abdominal and lower limb surgery under subarachnoid block with expected surgical time of 60-180 minutes were included in this study. Patients with contraindication to central neuraxial block, known hypersensitivity to any of the study drugs, pregnant women, known comorbid illness, patients converted to general anaesthesia were excluded from the study.

A computer generated randomization was used to number the patients and also to divide into Group BB and Group BN groups. Written informed consent was obtained from all. As institutional protocol, patients were kept nil orally for six hours prior to surgery, received premedication a day prior to surgery; Tab. Ranitidine 150 mg, Tab. Ondansetron 8 mg and Tab. Alprazolam 0.25 mg in the night. In all the patients baseline heart rate (HR), blood pressure (BP) and respiratory rate (RR) were measured and recorded. After shifting to the operating theatre, intravenous access (IV) was secured with 18 gauge IV cannula and preloaded with ringer lactate 10 ml/Kg for 20 minutes. In group BN patients received 15 mg of 0.5% hyperbaric bupivacaine plus 0.8 mg nalbuphine and in group BB, patients received 15mg of 0.5% hyperbaric bupivacaine plus 60mcg buprenorphine. SA was performed in all patients in sitting position using 25G Quinckies spinal needle at L3-L4 or L4-L5 level under aseptic precautions. The study medicament was administered over 10-15sec. Patient moved to supine position immediately after administering spinal block. Completion of injection was taken as zero time of induction of anaesthesia. Preparation of drugs was done by an independent anaesthesiologist who did not involve in the study and the drug mixture was administered by another anaesthesiologist who was blinded and performed a subarachnoid block.

For all the patients following parameters were studied. The onset of sensory and motor block, duration of sensory and motor block, duration of analgesia, intraoperative modified Ramsay sedation score, postoperative pain score using visual analogue scale, HR, systolic blood pressure (SBP) and diastolic blood pressure (DBP) and oxygen saturation (SpO2) and side effects (hypotension, bradycardia, and respiratory depression) were recorded. Hypotension was defined as decrease of systolic BP by more than 20% from baseline and treated with intravenous fluids and incremental doses of vasopressors when it was required. Bradycardia was defined as HR < 60 beat/min and was treated with injection atropine 0.6mg intravenously. Sensory block was assessed by loss of sensation to pinprick using 23-G sterile needle. Onset or induction of sensory block was the time from intrathecal injection administration to loss of pinprick sensation at T10 segment.

Duration of sensory block defined as the time to two segment regression time from the highest level of the sensory blockade. Motor block assessment was initiated immediately after intrathecal injection by using modified Bromage scale [7]. Onset of motor block was taken as time to achieve modified Bromage score 3 from the time of subarachnoid blockage injection. Thereafter, motor block regression was noted and duration for complete motor block recovery was taken as the time from subarachnoid injection to return of Bromage score to zero. Post-operative analgesic was intravenous 100 mg tramadol administered after noting the time when the patient complained of pain (VAS score 4). Duration of analgesia was taken as time between spinal injection to the request of first rescue analgesia.

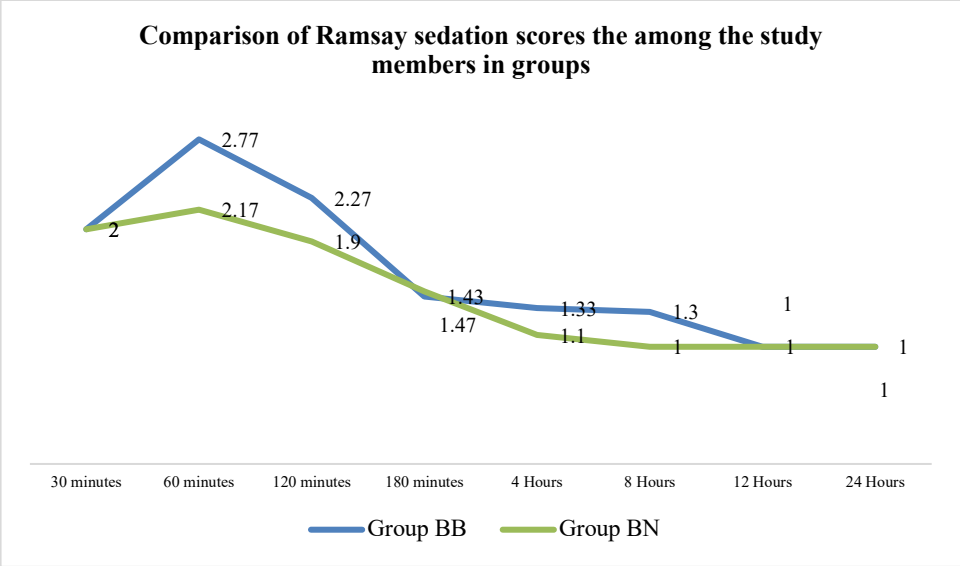
Continuous variables were presented as mean ± standard deviation (SD). Categorical data was compared using the Chi-square or Fisher's exact test. Continuous variables were compared using Independent t-test. All tests were two-tailed and at 95% confidence interval and 5% alpha level; $P \leq 0.05$ was considered to be statistically significant.

Results

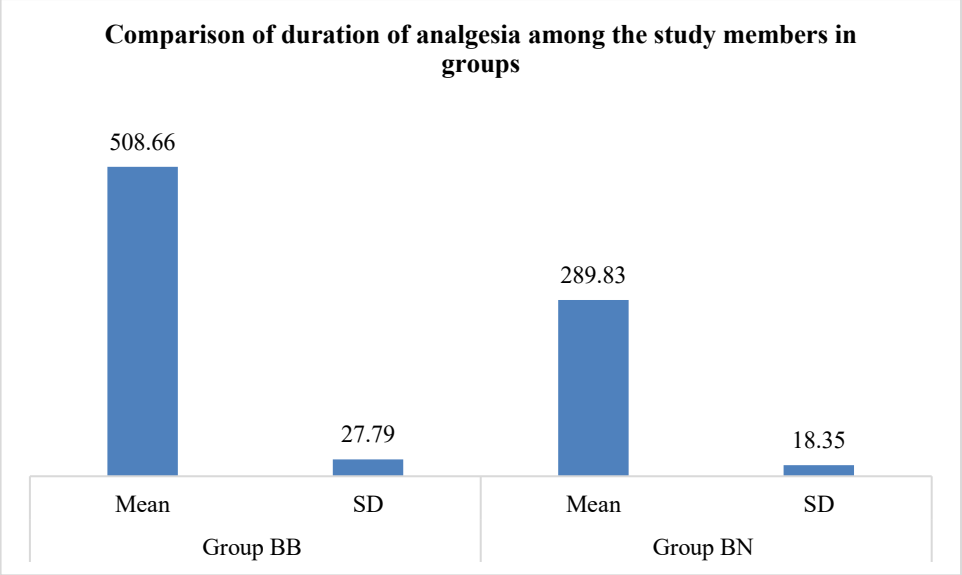
Total 60 patients were included, 30 per group. In group BB 16 (53.33%) were male and it was 18 (60%) in group BN; P=0.795. The mean age, height, weight, duration of surgery and vitals in both groups were comparable (P>0.05). There was no significant fall in the BP and HR in both groups during the entire intraoperative and postoperative period (Table 1). Statistically there was significant difference respectively in the mean onset of sensory block, mean motor block, mean duration of sensory block, motor block was significantly prolonged in group BB compared group BN (Table 2). The mean Ramsay sedation scores at 60^{th}, 120^{th}minutes, four and eight hours were significantly low in group BN (Graph 1)**.** The mean duration of analgesia was significantly prolonged in group BB (508.66±27.79 vs 289.83±18.35 minutes; P<0.001) (Graph 2). Five (16.67%) patients had postoperative nausea vomiting in group BB and just 2 (6.67%) in group BN; the difference was statistically not significant (P=0.212) (Graph 3).

Table 1: Demographic and hemodynamic profile of patients using different adjuvants for SA					
Variable	**Group BB**		**Group BN**		**P value**
	Mean	**SD**	**Mean**	**SD**	
Age	43.33	11.76	39.6	11.28	0.215
Height in cms	165.3	6.56	165.83	6.26	0.748
Weight in Kg	65.13	7.06	65.07	8.79	0.974
Duration of surgery	109	25.51	105	27.85	0.564
Pulse rate**	76.03	8.05	79.87	9.88	0.105
SBP in mmHg	124.33	13.05	126.33	9.64	0.502
DBP in mm Hg	73.33	6.06	74.67	8.19	0.477
MAP in mmHg	85.3	6.17	88.3	7.85	0.106
Oxygen saturation %	99	0.64	99.27	0.52	0.083
RR per minute	15.87	1.33	16.2	1.47	0.362
* in minutes; **per minute;					

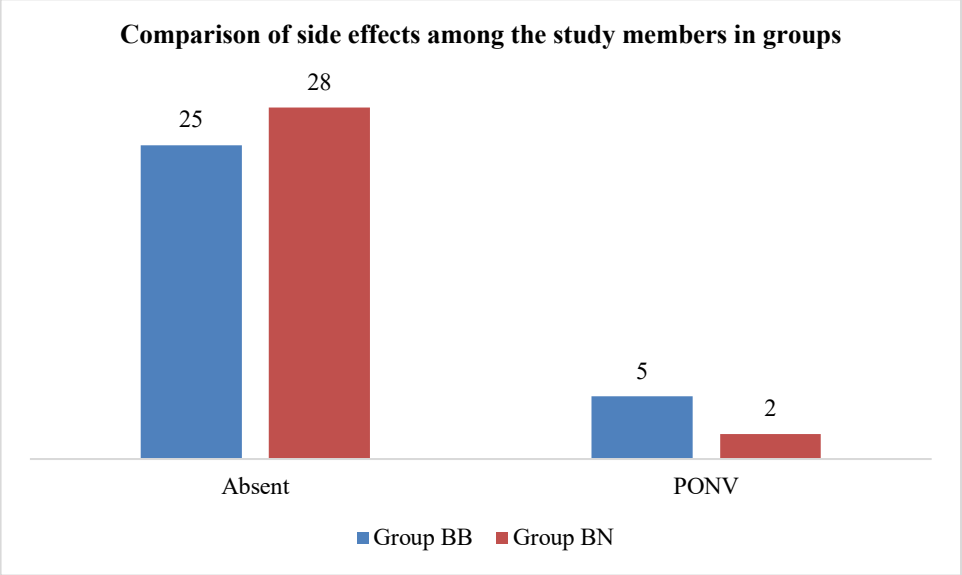
Table 2: Comparison of onset and duration of sensory and motor block in minutes among the study members in groups					
Parameters	**Group BB**		**Group BN**		**p value**
	mean	**SD**	**mean**	**SD**	
Onset of sensory block	3.66	0.49	2.52	0.41	<0.001
Onset of motor block	5.7	0.7	4.5	0.74	<0.001
Duration of sensory block	236.67	13.67	169.17	12.6	<0.001
Duration of motor block	419.83	15.56	252.87	15.61	<0.001



Graph 1: Comparison of Ramsay sedation scores the among the study members in groups



Graph 2: Comparison of duration of analgesia among the study members in groups



Graph 3: Comparison of side effects among the study members in groups

Discussion

The present study compared intrathecal nalbuphine and intrathecal buprenorphine as adjuvants to hyperbaric bupivacaine for POA in patients undergoing lower limb surgeries under SA. Subarachnoid block remains one of the most commonly used anaesthetic techniques for lower limb procedures because it provides rapid onset, dense sensory and motor blockade, reliable surgical conditions and good perioperative haemodynamic stability. However, the limited duration of bupivacaine-induced POA often necessitates the use of intrathecal adjuvants. Opioid adjuvants enhance spinal analgesia by acting on opioid receptors in the substantia gelatinosa of the dorsal horn, thereby inhibiting nociceptive transmission through A-delta and C fibres without producing major impairment of sympathetic function. In the present study, both nalbuphine and buprenorphine were clinically useful adjuvants, but their block characteristics differed. Nalbuphine produced earlier onset of sensory and motor blockade, whereas buprenorphine produced significantly prolonged sensory block, motor block, duration of analgesia and time to first rescue analgesic. These observations are consistent with the pharmacological differences between the two agents and support the continued clinical interest in identifying the most appropriate opioid adjuvant for SA in lower limb surgeries [1, 8].

In the present study, haemodynamic parameters were comparable between the nalbuphine and buprenorphine groups, and no clinically significant instability in HR, SBP, DBP or oxygen saturation was observed. This finding is important because intrathecal adjuvants should ideally prolong analgesia without increasing hypotension,

bradycardia, respiratory depression or delayed recovery. Kaushal et al. also reported that intrathecal buprenorphine and nalbuphine, when combined with heavy bupivacaine for lower limb orthopaedic surgeries, provided effective SA with negligible adverse effects and without clinically important haemodynamic compromise [1]. Similar safety observations were reported in studies evaluating nalbuphine with hyperbaric bupivacaine, where nalbuphine improved perioperative analgesia while maintaining acceptable haemodynamic stability [3, 9]. The absence of respiratory depression in the present study is particularly relevant because respiratory depression is one of the feared complications of neuraxial opioids. Nalbuphine, being a κ-opioid receptor agonist and μ-receptor antagonist, has a ceiling effect for respiratory depression, while buprenorphine, despite strong μ-receptor affinity, has been used safely in low intrathecal doses [10, 11]. Therefore, the haemodynamic and respiratory safety profile observed in this study supports the feasibility of using either drug as an intrathecal adjuvant in carefully selected ASA I–II patients undergoing lower limb surgeries.

The onset of sensory block and motor block was significantly earlier in the nalbuphine group than in the buprenorphine group. In the present study, the onset of sensory block was 2.52±0.41 minutes in group BN compared with 3.66±0.49 minutes in group BB, while the onset of motor block was 4.50±0.74 minutes in group BN compared with 5.70±0.70 minutes in group BB. This suggests that nalbuphine may be preferable when early establishment of surgical anaesthesia is desired. Similar findings have been reported in trials comparing nalbuphine with other intrathecal opioids, where nalbuphine showed faster onset of sensory and motor blockade and improved early intraoperative analgesic profile [12, 13]. In contrast, Kaushal et al. observed comparable onset of sensory and motor block between nalbuphine and buprenorphine groups, indicating that onset characteristics may vary according to dose, baricity, study population, type of surgery and assessment method [1]. The faster onset with nalbuphine in the present study may be explained by its effective spinal κ-receptor-mediated antinociceptive activity and possible synergistic interaction with bupivacaine at the dorsal horn level. However, while early onset is beneficial for operating room efficiency, it should be interpreted along with duration of block and postoperative analgesic efficacy, because the overall value of an intrathecal adjuvant depends not only on how quickly the block begins but also on how long effective analgesia is sustained [2].

The duration of sensory and motor blockade was significantly longer in the buprenorphine group than in the nalbuphine group. The mean duration of sensory block was 236.67±13.67 minutes in group BB compared with 169.17±12.60 minutes in group BN, while motor block lasted 419.83±15.56 minutes in group BB compared with 252.87±15.61 minutes in group BN. This finding agrees with Kaushal et al., who concluded that intrathecal buprenorphine was superior to nalbuphine as an adjuvant to 0.5% bupivacaine in lower limb orthopaedic surgeries because it provided longer sensory block and delayed need for rescue analgesia [1]. Borkotoky et al. also demonstrated that buprenorphine in combination with bupivacaine prolonged POA, with dose-dependent improvement in analgesic duration [4]. The prolonged block with buprenorphine may be explained by its high lipid solubility, strong receptor affinity, slow dissociation from opioid receptors and combined spinal and supraspinal analgesic actions. These properties allow buprenorphine to remain active for a longer duration at receptor sites, resulting in sustained analgesic benefit. However, prolonged motor block may delay early mobilisation in some patients; therefore, buprenorphine may be more suitable for procedures where prolonged POA is desirable and delayed ambulation is clinically acceptable. In contrast, nalbuphine may be preferred when faster onset and shorter motor recovery are desired.

POA was the most clinically relevant outcome of this study. The mean duration of analgesia was significantly prolonged in the buprenorphine group compared with the nalbuphine group, 508.66±27.79 minutes versus 289.83±18.35 minutes, and the time to first rescue analgesia was similarly prolonged, 516.00±27.95 minutes versus 294.83±18.35 minutes. This nearly two-fold increase in analgesic duration indicates that buprenorphine provided superior postoperative pain control when added to intrathecal bupivacaine. These findings are supported by studies showing that intrathecal buprenorphine improves POA and reduces early rescue analgesic requirement [4, 14]. Studies comparing nalbuphine with fentanyl have also shown that nalbuphine is an effective intrathecal adjuvant and provides longer analgesia than fentanyl in several settings, confirming that nalbuphine is clinically useful, although in the present study it was less effective than buprenorphine for prolonging analgesia [12,13,15]. A randomised comparative study on intrathecal nalbuphine also concluded that nalbuphine added to local anaesthetics significantly prolongs sensory regression and analgesic duration, with an acceptable adverse-effect profile [16]. Thus, the present findings should not be interpreted as nalbuphine being ineffective; rather, buprenorphine demonstrated greater analgesic prolongation in this specific comparative setting.

The adverse-effect profile was acceptable in both groups. Postoperative nausea and vomiting (PONV)

were slightly more frequent in the buprenorphine group, but the difference was not statistically significant. No pruritus, respiratory depression, desaturation, euphoria or dysphoria was observed in either group. This supports the clinical safety of both agents when administered in appropriate intrathecal doses. Similar studies have reported low rates of serious adverse effects with intrathecal nalbuphine and buprenorphine when used with bupivacaine [1,4,9,17]. The mild increase in nausea and vomiting with buprenorphine may reflect μ-receptor-related opioid activity, whereas nalbuphine may have a lower incidence of μ-mediated adverse effects due to its antagonist action at μ receptors [10, 16]. The present study has certain limitations. It was conducted in a single centre with a relatively small sample size, and only one dose of each adjuvant was evaluated. Different surgical subtypes, duration of surgery, postoperative mobilisation, patient satisfaction and longer follow-up pain scores were not analysed in detail. Future multicentre trials with larger sample sizes, dose-response comparisons and functional recovery outcomes are required. Overall, the present study indicates that intrathecal buprenorphine with hyperbaric bupivacaine provides longer sensory and motor blockade and superior POA, while intrathecal nalbuphine provides earlier onset of sensory and motor blockade with good safety. Therefore, buprenorphine may be considered when prolonged POA is the priority, whereas nalbuphine may be useful when faster onset and fewer μ-mediated adverse effects are desired [1,16].

Conclusion: The present study concluded that both intrathecal nalbuphine and intrathecal buprenorphine were effective adjuvants to hyperbaric bupivacaine for lower limb surgeries under SA. Nalbuphine produced a faster onset of sensory and motor blockade, making it useful when early block establishment is desired. However, buprenorphine provided significantly longer sensory and motor blockade, prolonged postoperative analgesia, and delayed requirement of rescue analgesic compared with nalbuphine. Haemodynamic stability was maintained in both groups, and adverse effects were minimal and comparable. Thus, intrathecal buprenorphine appears superior for prolonged postoperative analgesia, while nalbuphine offers earlier onset with good safety.

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